(c) a second cationic and water-soluble functional monomer. In the process, the sample is brought into contact with an adsorption reagent comprising a discontinuous phase of the particulate support in an aqueous continuous phase to adsorb the nucleic material onto the particulate support.

In the contacting step of the present invention, the reaction medium has a pH at most equal to 7, an ionic strength at most equal to 10^{-2} M, and a temperature less than the LCST of the polymer. As demonstrated in Example 2 of the present application, in addition to temperature, the pH and the ionic strength of the reaction medium have a significant effect on the ability of the nucleic material to be adsorbed by the polymer material. In particular, at acidic pH, the polymer particles, which contain cationic monomers, are widely positively charged. As a result, the negatively charged nucleic acids attach to the particles via electrostatic forces. See Figure 2. In addition, as demonstrated in Figure 4, the attractive electrostatic forces between the negatively charged nucleic material and the positively charged polymer surface decreases with the increase in ionic strength. As a result, there is a decrease in the attachment of the nucleic material to the polymer with an increase in ionic strength.

Itoh is directed to a high molecular composite material having, as one component thereof, a homopolymer or copolymer of an N-substituted derivative of acrylamide or methacrylamide. Page 1, lines 2-6. As a comonomer, Itoh teaches hydrophilic monomers, ionic monomers and hydrophobic monomers. Examples of ionic monomers provided in Itoh include acids and amines. Page 7, lines 4-24. Itoh teaches eight potential methods to insolubilize the polymer. Included among these eight techniques is the use of a cross-linkable monomer. Page 13, line 25 - page 14, line 5. However, Itoh provides no motivation to select

a cross-linked polymer containing ionic monomers, must less containing cationic monomers, from the large group of homopolymers and copolymers taught therein.

In addition, Itoh teaches that the polymeric material permits the formation of composite materials with a very large number of low molecular or high molecular compounds. Page 4, lines 7-10. Among such compounds, Itoh teaches compounds containing active hydrogen and compounds containing hydrophobic groups. Page 19, lines 17-20. Itoh then goes on to list various compounds that can be attached to the polymer from page 19, line 23, to page 32, line 14. Included in Itoh at page 45, lines 3-4, is a passing reference to nucleic acids as being an example of a compound substituted by groups containing active hydrogen atoms. However, Itoh does not include an example demonstrating appropriate conditions at which nucleic acids can be attached to the polymer.

Itoh teaches at least two distinct methods for holding and releasing the various compounds from the polymer. With regard to compounds substituted by groups containing active hydrogen atoms, such as nucleic acids, Itoh teaches that the compounds develop intermolecular forces such as hydrogen bonds, hydrophobic bonds or the like with the homopolymers or copolymers. Page 44, lines 22-25. Thus, Itoh teaches that "[t]hese compounds may be held at high temperatures and released at low temperatures." Page 45, lines 11-13. This teaching suggests the use of higher temperatures for holding nucleic acids, thus teaching away from temperatures less than the LCST of the polymer, as recited in the present claims.

In a totally separate technique for holding components to the polymer, Itoh teaches utilizing the property of the homopolymers or copolymers taught therein to absorb and hold water upon contact with aqueous solutions but, when heated, shrink and release water. Page 44, lines 3-6. In this technique, the homopolymers or copolymers may be heated to

release the components, which must be low molecular weight compounds. Page 46, lines 4-8. In addition, the shrink and swell property of the polymer can also be utilized in a technique in which the low molecular compounds are held at high temperatures and released at low temperatures. Page 47, lines 16-18. However, Itoh makes no mention of utilizing the shrink and swell properties of the polymers to hold nucleic acids to the polymer. Thus, Itoh clearly does not teach or suggest whether nucleic acids are held at high temperatures and released at low temperatures or held at low temperatures and released at high temperatures based on the shrink and swell of the polymer. As a result, this teaching provides no indication as to whether high or low temperatures should be utilized in holding nucleic acids to the polymers. In particular, Itoh does not teach or suggest utilizing temperatures less than the LCST of the polymer to hold nucleic acids to the polymer by its shrink and swell property.

In addition, Itoh does not teach or suggest appropriate pH and/or ionic strength conditions for holding nucleic acids to the polymers of the present invention, which contain cationic monomers. As demonstrated in Example 2 of the present application, these forces have a significant affect on whether the polymer is able to hold the nucleic material. Although Itoh teaches that there may be a relationship between the pH of the system and whether the components are held to or released by the polymer, Itoh does not teach or suggest how the various techniques for holding various components to the polymer are affected by changes in the pH. In particular, Itoh does not teach or suggest how pH affects the ability of the polymer to hold nucleic acids. In addition, Itoh does not teach or suggest how pH will affect the ability of polymers containing cationic monomers to hold nucleic acids at temperatures below the LCST of the polymer.

In summary, the claimed invention is directed to the use of a particular reaction medium and the use of a particular polymer in order to isolate nucleic material from a sample.

Itoh does not provide any motivation to select the particular features recited in the claimed invention in order to isolate nucleic material. In particular, Itoh does not teach or suggest selecting a pH at most equal to 7, an ionic strength at most equal to 10^{-2} M, and a temperature less than the LCST of the polymer, as well as the use of a cationic monomer in the particulate polymer, to isolate nucleic material from a sample.

Hoffman is directed to methods for delivering substances into, removing substances from, or reacting substances with a selected environment utilizing polymer gels or coatings exhibiting either an upper or lower critical solution temperature. Column 1, lines 16-22. As polymers having an LCST, Hoffman teaches substantially hydrophobic polymers of N-substituted acrylamides or methacrylamides, hydroxy alkyl cellulose, polyoxazolidone, polyvinylmethylether, polyethylene oxide, polymethacrylic acid, or copolymers thereof. Column 4, lines 31-38. Hoffman does not teach or suggest a copolymer of an acrylamide or acrylamide derivative monomer with a cationic functional monomer.

To bind a component that is part of an affinity binding pair, such as DNA or RNA, Hoffman teaches physically or chemically binding the other binding component, namely, complementary DNA or RNA, to the polymer. The polymer gel/binding component is then contacted with a solution containing the second component of the binding pair. The mixture is then incubated at a temperature sufficient to cause the polymer gel to absorb liquid from the solution containing the second binding component, thereby allowing the second binding component to specifically bind to the first binding component. Column 4, line 57 - column 5, line 19. Hoffman does not teach or suggest relying merely on the absorption of the DNA or RNA to the polymer to remove the DNA or RNA from the sample.

In addition, Hoffman provides no teaching or suggestion of using a pH at most equal to 7 and an ionic strength at most equal to 10^{-2} M. Although Hoffman teaches that buffer

salts surrounding the solution make it easier to deliver methylene blue on heating above the LCST at column 15, lines 53-56, Hoffman provides no teaching or suggestion as to how the above-mentioned method for holding DNA or RNA to its binding pair on the polymer would be affected by a pH at most equal to 7 and an ionic strength at most equal to 10^{-2} M. Therefore, one of ordinary skill in the art would not have been motivated by the teachings of Hoffman to select a reaction medium in which the pH is at most equal to 7 and the ionic strength is at most equal to 10^{-2} M.

Even if combined, Itoh and Hoffman do not teach or suggest the present method. In particular, Hoffman is directed to techniques of holding substances to a polymer gel by the swell and shrink property of the gel. Thus, assuming any combination is proper, Hoffman can only be properly combined with teachings of Itoh directed to holding substances to the gel based on the shrink and swell properties of the gel. At least these teachings of Itoh do not provide any motivation to select a pH at most equal to 7. In addition, Itoh does not provide any motivation to select a cationic comonomer for the particulate polymer or an ionic strength at most equal to 10^{-2} M. Therefore, Itoh does not overcome the deficiencies of Hoffman.

Kawaguchi is directed to a DNA-immobilized microsphere comprising DNA chains having base sequences that bind to a specific protein. In Kawaguchi, the immobilization of DNA chains on the surface of the particles is obtained by a covalent bonding method. Column 4, lines 66-68. Kawaguchi teaches the use of a buffer solution having a high salt concentration to release the proteins from the DNA. Column 5, lines 51-54. However, the ionic strength at which proteins bind to and are released from DNA provides no indication of appropriate ionic strengths for holding nucleic material to the polymer. Thus, Kawaguchi does not overcome the deficiencies of Itoh and/or Hoffman.

In addition, Kausch is directed to a method for the isolation and sorting of biological materials comprising anchoring the biological material to a support to immobilize it, labeling the biological material with a binding composition that is capable of binding to it, the composition also being attached to magnetic particles, and isolating individual components of the biological material by reversal of the immobilization step and exposure to a magnetic field. The Office Action states that the binding reaction took place in low ionic strength buffers and the release was affected with high ionic strength buffers. Upon review of Kausch, however, in particular columns 3-10 noted in the Office Action, although it appears that Kausch teaches the use of high salt concentrations to remove the binding composition and the magnetic particles from the biological material, Kausch does not teach or suggest that high salt concentrations can be used to remove the biological material from the support, much less from the polymers of the present invention. Therefore, Kausch does not overcome the deficiencies of Itoh and/or Hoffman.

None of the cited references alone or as combined teach or suggest the present invention. Therefore, the rejection under 35 U.S.C. §103 should be reconsidered and withdrawn.

In view of the above remarks, it is respectfully submitted that the above-identified patent application is in condition for allowance. Favorable consideration and prompt allowance are therefore respectfully requested.

Should the Examiner believe anything further would be desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

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